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09/766,399	01/19/2001	Wesley B. Bruce	1165	7368

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EXAMINER

EINSMANN, JULIET CAROLINE

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 06/19/2002

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/766,399

Applicant(s)

BRUCE ET AL.

Examiner

Juliet Einsmann

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 May 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 17 and 18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 January 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4,5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, particularly the sequence disclosed in claim 1(c), in Paper No. 8 is acknowledged. The traversal is on the ground(s) that the MPEP allows for up to ten independent and distinct nucleotide sequences to be examined (MPEP 803.04). This is not found persuasive because as a first point, claim one is not limited to only ten independent and distinct nucleotide sequences, as the elements listed can be provided in any order in any of the constructs listed. Thus, for invention 1(c), the claim actually encompasses fifteen factorial sequences. Furthermore, although the MPEP allows, at the examiner's discretion, for the examination of up to ten nucleic acid sequences in a single application, it is determined by the examiner that in this case such an allowance would pose too large a burden on the search facilities of the office and on the examiner to review the searches. For each of the distinct promoters in this case a separate search is required of both the sequence databases and the textual literature databases. The requirement is still deemed proper and is therefore made FINAL.

2. Examined herein are claims 1-16, with regard to the promoter defined in 1(c). Furthermore, the portion of the claims that refers to nucleotide sequences that hybridize to 1(c) and that are variants of 1(c) have also been considered. The promoter defined in 2(c) is a particular embodiment of 1(c) and has been considered as well as a promoter comprising instant SEQ ID NO: 65.

Drawings

3. The drawings are approved by the examiner as being acceptable for examination.

Claim Objections

4. Claims 2-6 and 8-15 are objected to because of the following informalities:

The claims are objected to because they refer to the drawings in section (i) of the claims. MPEP 2173(s) states "Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." In the instant case the drawings contain sequences which can be concisely identified by sequence identifiers.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-6 and 8-16 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6 and 8-16 are indefinite over the recitation of certain phrases in parentheses. These claims are indefinite because it is not clear how the information in parentheses is meant to be limiting to the claim. For example, in claim 1 part (c), the recitation "DRE 1 (SEQ ID NO: 59)", it is not clear if the "DRE 1 element" must comprise or consist of SEQ ID NO: 59, or if this is merely an example of one DRE 1 element encompassed by the claims. This ambiguity exists each time a sequence identifier appears in parentheses and it is not clear if applicants are

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intending to particularly require the recited sequence in the claims or if applicants are merely providing this as one example of the generically described sequences. Amendment of the claim to recited, for example, "wherein the DRE 1 promoter element consists of SEQ ID NO: 59", or some other similar language would clarify this issue.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for plant promoters comprising synthetic multimeric promoter element regions (SMPER) consisting of instant SEQ ID NO: 66, 67, 65, 68, 69, 71, 72, and 70, does not reasonably provide enablement for any SMPER, or SMPER that are identified merely by the combination of elements contained therein, or SMPER sequences that are modified from the recited sequence identifiers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

A restriction requirement has been applied to the instantly rejected claims requiring that Applicant elect a single promoter sequence. Applicant's election of the sequence disclosed in 1(c) is acknowledged. For the purposes of examination under 112 1st paragraph, the entire scope of the disclosure in the specification has been considered. Particular discussion in this rejection will focus on the elected promoter.

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Claim 1 is drawn to plant promoters that comprise at least one SMPER having a nucleotide sequence, wherein the nucleotide sequence comprises a number of promoter elements, as recited in the claims. For example, the elected claim requires that the promoter have five DRE 1 elements, three ABRE1 elements, two AS-1 elements, and five GT-2 elements. Thus, the number of combinations encompassed by claim 1(c) is fifteen factorial, or 1,307,674,368,000. Part (i) of claim 1 further provides "a nucleotide sequence that hybridizes under stringent conditions to any of the nucleotide sequences" previously recited in the claim. Claim 2 (c) requires that the recited elements be provided in a particular sequential order, while sections (j) and (k) of claim 2 allow for a sequence that comprises a "variant" of a particular sequence or that hybridizes under stringent conditions to the recited promoters. Claims 4-6 depend from claim 2 and recite chimeric genes, transformation vectors and plants. Claim 7 is drawn to a plant or plant part having stably incorporated into its genome a DNA construct comprising a plant promoter operably linked to a coding sequence, wherein the plant promoter comprises at least one SMPER. Claim 8 recites a plant or plant part having stably incorporated into its genome a DNA construct comprising a plant promoter operably linked to a coding sequence, wherein the plant promoter comprises a nucleotide sequence of the same scope as those described in claim 2. Claims 9-11 depend from claim 2 and further limit the species of the plants. Claim 12 is drawn to plant cells having stably incorporated into its genome a DNA construct comprising a plant promoter operably linked to a coding sequence, wherein the plant promoter comprises a nucleotide sequence of the same scope as those described in claim 2. Claims 13-15 depend from claim 12. Claim 16 depends from claim 1 and is a method for expressing a heterologous nucleotide sequence in a plant using a promoter as claimed in claim 1.

The specification teaches that certain promoter elements have strong binding activity with maize nuclear extracts (Example 1). The specification teaches that these elements were randomly combined to make promoters, and that 17 were tested in experiments where maize was transformed with a construct comprising the promoters (Examples 3-4). The experiments demonstrated that of the 17 SMPER promoters tested, nine resulted in the promotion of LUC activity in transgenic maize. The promoter herein disclosed as SEQ ID NO: 65 is one of the nine promoters that demonstrated activity in maize.

The prior art teaches many constructs for the expression of heterologous genes in plants. Many of these fall within the scope of the broad definition of SMPER provided in the specification, and to the extent that the prior art falls within the scope of the instant claims, the claims are enabled for that scope. This rejection is particularly applied to the rejected claims to address claims which require the elements recited in claim 1(c) in any order, variants of SEQ ID NO: 65, and sequences that hybridize to 1(c) or 2(c).

The ability of a promoter to function is highly sequence specific. The art teaches repeatedly that mutations in a critical region of a promoter element can destroy the ability of a construct to function in promotion. For example, Pietrkowski *et al.* (Experimental Cell Research, 193, 283-290 (1991)) teaches that when synthetic promoters were produced wherein the sequence of an enhancer element was mutated, little to no promotion was observed from the constructs where the promoter was mutated (see for example Figure 6). Chan *et al.* (Plant Molecular Biology 46 :131-141, (2001)) mutation in a critical XXIII element of the GAPB promoter abolished transcription completely (Figure 6), while mutations in other elements did not abolish activity (Figure 6). Thus, it is evident that it is highly unpredictable how promoter

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elements will respond to even very minor sequences changes. In addition, the order that promoter elements occur in a construct has an effect on the functionality of the promoter. Omilli *et al.* (Molecular and Cellular Biology, June 1986, p. 1875-1885) teach that the relative arrangement of promoter elements is a critical factor contributing to the activity of the promoter (ABSTRACT, for example).

The specification underscores this unpredictability by demonstrating that of 17 SMPER constructs produced, only nine of them were able to promote expression of a marker gene in maize. And even similar promoters containing similar numbers of elements, for example A56 and A51 which have the same number of elements, do not have the same response. That is, A51 was able induce LUC activity, while A56 was not. There is no clear pattern as to which sets of elements work or how to predict on its face if a set of elements will be able to promote expression.

With regard to the claimed and elected invention, there is only a single working example in a genus that contains hundreds of millions of possible promoter constructs which have been modified by any number of deletions, insertions, order changes, and rearrangements, that working example being a promoter comprising SEQ ID NO: 65. With regard to claim 1(c), while the claim requires the presence of particular elements, it does not require them in a particular order. The specification does not provide any guidance as to how the elements can be rearranged from the order of SEQ ID NO: 65 and still result in a functional promoter. With regard to the elements of the claims that allow for sequences that "hybridize to" or are "variants" of the recited promoters and elements, such claims encompass promoters comprising elements that are modified from the elements taught in the instant specification. However, the

specification does not provide any examples of such sequence, nor does the specification particularly teach how the elements in the promoter of claim 1(c) or 2(c) can be modified and still retain its ability to promote transcription. In light of the sequence specificity required for promoter activity, and the high degree of unpredictability with regard to the ability to change the sequence of a promoter element and have it retain its functionality, such guidance would be necessary to one to make and use the claimed invention.

The practice of the claimed invention commensurate in scope with the claims would require the construction and screening of hundreds of millions of possible promoters that comprise the elements recited in claim 1(c) in any order, or that hybridize to those elements, or that are variants of the promoter recited in SEQ ID NO: 65, or that hybridize to the promoter described in claim 2(c). The construction and screening of all of these possible promoters to determine the functional promoters would require undue experimentation because there is absolutely no way to predict which promoters would be functional in light of the high level of sequence specificity in promoter sequences.

Thus, in light of the broad scope of the claims, the high level of unpredictability in the promoter art, the lack of examples and direction provided in the specification, and the high level of experimentation necessary to practice the claimed invention, it is concluded that undue experimentation is necessary to practice the claimed invention commensurate in scope with the instant claims.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishige *et al.* (EP 0754757 A2).

Ishige *et al.* teach a plant having stably incorporated into its genome a DNA construct comprising a plant promoter operably linked to a coding sequence, said plant promoter comprising at least one synthetic multimeric promoter element region (SMPER) that enhances expression of said coding sequence (Examples 4, 5, and 6, page 6). The promoters used by Ishige *et al.* meet the definition of a SMPER provided in the specification because they contain more than one promoter element in an arrangement not found in nature (see specification, page 4, lines 24-27). For example, the construct called Gbox10/-90/GUS have a “Gbox” element linked to the minimal region of the cauliflower mosaic virus 35S promoter.

This reference is applied to claims 1-6 and 7-16 insofar as they are drawn to include the elected promoter that is 1(c)) and also “a nucleotide sequence that hybridizes under stringent conditions” to the nucleotide sequence of (c), or in claim 2, a nucleotide sequence that hybridizes to or is a variant of the nucleotide sequence of (c). The teachings of Ishige *et al.* meet the limitations of these claims. The promoters taught by Ishige *et al.* all contain the minimal region of the cauliflower mosaic virus 35S promoter, which is taught in SEQ ID NO: 3 of the disclosure of Ishige *et al.* The promoter element disclosed herein and called “AS-1” is identical to nucleotides 4-31 of the sequence taught by Ishige *et al.* as SEQ ID NO: 3. Thus, the promoters

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taught by Ishige *et al.* are constructs that comprise at least one synthetic multimeric promoter element region having a nucleotide sequence that hybridizes under stringent conditions to the nucleotide sequence of (c). The promoters taught by Ishige *et al.* meet the limitations of claim 1 or 2 because they comprise elements that would hybridize under stringent conditions to the instantly disclosed and claimed promoter of section (c). Furthermore, Ishige *et al.* teach a chimeric gene comprising the promoter operably linked to a coding sequence (GUS), an expression cassette, a transformation vector, and plants stably transformed with the transformation vector. Ishige *et al.* exemplify a dicot plant and a monocot plant (tobacco and rice), and further teach that the methods and vectors of their invention can be used with a wide variety of plants, including maize (p. 4, line 31).

Conclusion

11. A plant promoter comprising a synthetic multimeric promoter element region that consists of SEQ ID NO: 65 is free of the prior art. A claim so limited would be allowable.

12. Prior to allowance, non-elected subject matter will be required to be cancelled from the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the

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organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



JEFFREY FREDMAN
PRIMARY EXAMINER



Juliet C. Einsmann
Examiner
Art Unit 1634

June 11, 2002